HPV testing prevents more invasive cervical cancers than cytology

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Human papillomavirus (HPV) DNA testing prevents more invasive cervical cancer compared to cytology screening alone by detecting persistent high-grade lesions (which lead to cervical cancer) at an earlier time. As such, HPV testing should become the primary screening tool for women aged 35 years or older at longer screening intervals, with cytology reserved for triage of women who test positive for HPV, concludes an Article published Online First in The *Lancet Oncology*.

It is well established that DNA testing for HPV increases the detection of precancerous lesions called high-grade cervical intraepithelial neoplasia (CIN2 and CIN3) compared with cytology. But HPV testing is less specific and results in more false-positive tests than conventional Pap smears. However, it is not known whether shifting to HPV testing from standard cytology in cervical cancer screening programmes increases their effectiveness in preventing invasive cervical cancer, particularly in developed countries where advanced cervical cancers are rare among screened women.

The New Technologies for Cervical Cancer (NTCC) screening study, led by Guglielmo Ronco and colleagues from Italy, examines the benefits and risks of introducing HPV testing for cervical cancer screening and assesses the most appropriate age for initiating HPV testing.

Two rounds of screening were done for two separate recruitment phases in which women aged 25□□ years were randomly assigned to conventional cytology only or to HPV testing plus cytology (first phase) and HPV

testing alone (second phase).*

Findings showed that in the first round of screening a similar number of invasive cancers were detected in each group (nine in the cytology group vs seven in the HPV group). But in the second round no cancers were detected in the HPV group compared with nine in the cytology group—suggesting that HPV-based screening is more effective than cytology at preventing invasive cervical cancer, plausibly because of earlier detection and treatment of CIN.

Importantly, for women aged 35 years or older, combining HPV testing with cytology did not increase the sensitivity of screening indicating that increased detection of CIN3 was primarily due to HPV testing.

However, among younger women aged 25□□ years, HPV testing led to over-diagnosis and treatment of regressive CIN2 lesions which is associated with increased risk of pregnancy-related morbidity.

The authors say: "Our data support the use of stand-alone HPV testing as the primary screening test. The extremely low detection of CIN3 at round two in the HPV group (2 per 10 000) indicates that HPV-based screening at extended intervals is safe."

They conclude: "Further follow-up is needed to define how long screening intervals can be safely extended. Research is needed to define the optimum management of HPV-positive women…to minimise the costs related to increased referral to colposcopy and overdiagnosis of regressive lesions."

In an accompany Comment, Philip Castle and Hormuzd Katki from the National Cancer Institute in the USA conclude: "HPV testing shows a great deal of promise to revolutionise cervical cancer screening…We advocate that clinical management be based on estimating a woman's

individual risk of cervical precancer, rather than complex algorithms. Data from the current study could be used to develop risk estimates to make the promise of more effective and cost-effective cervical cancer prevention a reality."

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